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| EXAMINER | |
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| SHEN, WU CHENG WINSTON | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/529,011 | BRAUN, RALPH PATRICK | |
| | Examiner | Art Unit | |
| | WU-CHENG Winston SHEN | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02/19/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,7-10,12-14,16-19,21 and 26-53* is/are pending in the application.

4a) Of the above claim(s) *31-36 and 42-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7-10,12-14,16-19,21,26-30,37-41 and 45-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/19/2007 and 02/20/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's response received on 02/19/2008 has been entered. Claims 2, 4-6, 11, 15, 20, 22-25 are cancelled. Claims 1, 3, 7-10, 12-14, 16-19, 21, 26-53 are pending. Claims 1, 3, 7-10, 12-14, 16-19, 21, 37, 39, and 45-53 are amended.

Claims 31-36 and 42-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 3, 7-10, 12-14, 16-19, 21, 26-30, 36, 37-41, and 45-53 are currently under examination.

This application 10/529,011 filed on 08/02/2005 is a 371 of PCT/GB03/04218 09/29/2003 which claims benefit of 60/414,089 filed on 09/27/2002.

### *Claim Objections*

1. Previous objection of claims 26, 27, and 39 because of the following informalities: There is no article (i.e. "A") in the beginning of these claims, is ***withdrawn*** because Applicant's arguments have been fully considered and found persuasive.

Applicant argues that claims 26, 27 and 39 are directed to a plurality of coated particles, not a singular coated particle, as they refer to "Coated particles", and the claims in question are therefore submitted to be grammatically correct in their present form and do not require amendment.

2. Claim 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 36, 37-41, and 45-53 are objected because of the following informalities: **(i)** Claim 1 recites in step (d) "the endogenous gene expression regulatory units are different *to* one another" should and read "the endogenous gene expression regulatory units are different *from* one another"; **(ii)** Claim 1 recites in line 2 "where", which should read as "wherein"; **(iii)** Claim 1 recites "herpes virus genomic nucleic acid" in lines 2 and lines 3-4, which should read as "herpes viral genomic nucleic acid"; **(iv)** Claim 37 recites "herpes virus genomic nucleic acid" in line 3, which should read as "herpes viral genomic nucleic acid" . Claims 3, 7-10, 12-14, 16-19, 21, 26-30, and 45-53 depend from claim 1. Claims 38-41, depend from claim 37. Appropriate correction is required.

***Claim Rejection - 35 USC § 101***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Previous rejection of claims 1, 3, 7-10, 13-14, 16-19, 21, and 46-53 under 35 U.S.C. 101 because the claimed invention, independent claim 1, and their dependent claims 3, 7-10, 13-14, 16-19, 21, and 46-53, are directed to a non-statutory subject matter, is ***withdrawn*** because the claims have been amended. The rejection of claims 2 and 4 is ***moot*** because the claims 2 and 4 have been canceled.

The claims have been amended to recite the term "An isolated nucleic acid", and as amended the claims do not encompass non-statutory subject matter.

***Claim Rejection - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 37-41, and 45-53 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's arguments filed 02/19/2008 have been fully considered and they are partially persuasive. Previous rejection over claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 37-41, and 45-53 is ***maintained in part***, for the reasons of record advanced on pages 6-7 of the office action mailed on 04/19/2007. There are two aspects pertaining to this 112 second rejection and each aspect of the rejection is discussed in ***(i)*** and ***(ii)*** below. Previous rejection of claims 2 and 4 is ***moot*** because claims 2 and 4 have been canceled.

***Applicant's arguments and Examiner's response to Applicant's Arguments***

***(i) Applicant arguments*:** With regard to the reference to 80% sequence homology in the claims being unclear (page 6, paragraph 2 of the office action dated 04/19/2007), Applicant argues that the specification does provide illustrative examples of herpes viruses at page 28, second full paragraph and in original claim 7, and the Example 1 of the application refers to the specific HSV strain HG52 strain of HSV-2 as an illustrative example. Applicant also argues that the specification does not list the sequences of herpes viruses as these were publicly available as

of the priority date of the present application, as the skilled person would have been well aware, and it is also highlighted that the genomes of herpes viruses are substantial in size. In this regard, Applicant indicates that of HSV-2 is over 150 kb in length. Applicant further argues that to list the entire sequence of illustrative examples of known genome sequences for herpes viruses would therefore have made the specification unduly long, and the inclusion of the sequences was unnecessary, given the public availability of the sequences. Applicant provides a printout from the NCBI website in the supplemental Information Disclosure Statement filed herewith giving a summary for the entry for Genbank Accession Number Z86099, which corresponds to the entire sequence of the HSV-2 genome used in Example 1 and is included in the supplemental Information Disclosure Statement filed herewith. Applicant draws Examiner's attention to the literature publication, Dolan et al. (1998) *Journal of Virology*, 72(3): 2010-2021, which was also similarly publicly available and supplies the complete genomic sequence of HSV-2. Applicant indicates that this reference is also cited in the supplemental Information Disclosure Statement filed herewith, and the genomic sequences of herpes viruses were therefore publicly available at the time of the invention. Applicant concludes that the skilled person would therefore be able to compare a sequence to see whether or not it has at least 80% homology to such herpes virus sequences. Applicant also indicates that the specification goes into detail at pages 15 and 16 about how sequence homology can be calculated; the passages describe various algorithms and publicly available information for calculating sequence homology; sequence comparisons could be performed with sequences in databases; and the absence of the sequence of herpes viruses in the specification is not therefore does not preclude patentability.

***In response:*** Applicant's arguments are persuasive with respect to claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, and 45-53. The Examiner agrees with the Applicant with respect to the specification does disclose methods of measuring polynucleotide homology or identity on pages 15 and 16, and the existence of Genbank Accession Number Z86099, which corresponds to the entire sequence of the HSV-2 genome. The Examiner acknowledges that the phrase "at least 80% sequence homology to a herpes virus genomic nucleic acid" recited in claim 1, and the phrase "or has at least 90% homology to, the endogenous sequences of a herpes virus genome" recited in claim 51 are very broad, nevertheless clear. Therefore, the aspect of the rejection of claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, and 45-53 regarding the reference to 80% sequence homology in the claims being unclear under 35 U.S.C. 112, second paragraph, as set forth on pages 6 of the office action dated 04/19/2007 is ***withdrawn*** .

Applicant's arguments are not persuasive as they relate to claims 37-41. It is noted that the phrase "at least 80% sequence homology" recited in independent claim 37 is unclear as it fails to recite to what nucleic acid the 80% homology compared to. A standard for comparison must be recited in the claim. The rejection over claim 37 is not based on a lack of support in the specification but a lack of clarity as to what Applicant is claiming by the phrase "at least 80% sequence homology into a vector backbone". Claims 38-41 depend from claim 37.

Therefore, this ground of rejection is maintained over claims 37-41.

***(ii) Applicant's arguments***: With regard to the limitation "where the endogenous promoters of the units are active at the same phase in the herpes virus life cycle" being unclear (page 6 of the office action dated 04/19/2007), Applicant argues that the claims has been

amended and now recites "where the endogenous promoter of the units are all immediate early, all early or all late promoters". Applicant also cites Davido et al. (1996) Journal of General Virology, 77:1853-1863 as the support for such terminology used in the HSV art.

***In response*:** The Examiner agrees with the Applicant on that the terminology "immediate early, early or late promoters" is recognized in the filed of HSV research. However, the metes and bounds encompassed by the terminology are not explicitly disclosed in the specification, and the nomenclature used in HSV literature does not appear to have explicit consensus how these term encompasses are defined. In the specification, it discloses immediate early proteins such as ICP 0, 4, 22 and 27 (See paragraph [0151], US 2005/0272030, the publication of instant application). However, the metes and bounds of encompassed by the terms immediate early promoters, early promoters, late promoters are unclear as disclosed in the specification of instant application. In the HSV literature at the time of filing of instant application, promoters of HSV genes are also classified into α, β and γ promoters based on expression kinetics. For instance, **Rajcani et al.** discloses the following: The herpes simplex virus (HSV) has a 152 kbp dsDNA encoding probably 84 proteins. The approximate number of ORFs is 94, from which seven are doubled. During productive replication the cascade regulation of gene expression predominates, based on stepwise activation of immediate early (IE), early (E), early late (EL) and late (L) promoters. The promoters of different expression kinetic classes (α, β, γ-1 and γ-2) are equipped with different number of cellular transcription factor binding and/or enhancer motifs (See abstract, Rajcani et al. Peculiarities of herpes simplex virus (HSV) transcription: an overview, *Virus Genes*. 28(3):293-310, 2004). The ICP4 is classified as a α (IE) promoter (See Figure 1, page 295, Rajcani et al., 2004). Therefore, the amended

terminology "all immediate early, all early or all later promoters" recited in amended independent claims 1 and 37 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This aspect of the rejection of claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 37-41 and 45-53 under 35 U.S.C. 112, second paragraph, as set forth on pages 6 of the office action dated 04/19/2007 is ***maintained*** of the record.

5. Previous rejection of claims 3 and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is ***withdrawn*** because the claims have been amended..

***Applicant's arguments***: With regard to the limitation "expression regulatory units are immediate early genes" being unclear because regulatory units are not equivalent to genes (page 7 of the office action dated 04/19/2007), Applicant argues that the claims have been amended and now recites "wherein the endogenous gene expression regulatory units comprise immediate early promoters or early viral promoters". Applicant argues that gene expression regulatory units comprise promoters and hence the claims are clear.

With regard to claims 39-41 being unclear for being dependent on withdrawn claim 36 (page 7 of the office action dated 04/19/2007), Applicant argues that claim 39 has been amended to dependent from claim 38, instead of claim 36, and the status of claims 40 and 41 are marked as original, instead of withdrawn.

***In response***: The Examiner agrees with the Applicant in that gene expression regulatory units comprise promoters. Thereby, the aspect of the rejection pertaining to the previously

recited limitation "expression regulatory units are immediate early genes" recited in claim 3 is ***withdrawn***.

As amended, 38-41 depend from claim 37 and are currently under examination. Claims 39-41 no longer depend from claim 36, which is a withdrawn claim. The rejection of claims 39-41 in this regard is ***withdrawn***.

6. Previous rejection of claims 14 and 51 are rejected under 35 U.S.C. 112, second paragraph as there is insufficient antecedent basis for this limitation in the claim, is ***withdrawn*** because the claims have been amended.

***Applicant's arguments*:** With regard to claim 14 being unclear for reciting "the antigen" which lacks antecedent basis (page 7 of the office action dated 04/19/2008), Applicant argues that claim 14 has been amended to depend from claim 13, instead of claim 1.

With regard to claim 51 being unclear for reciting "the herpes virus genome" which lacks antecedent basis, Applicant argues that claim 51 has been amended to recite "a herpes virus genome".

***In response*:** The Examiner agrees with the Applicant on that claim 14, now amended to be dependent from claim 13, which provides the antecedent basis of the limitation "the antigen" recited in claim 14. Accordingly, the rejection directing to claim 14 in this aspect is ***withdrawn***.

Applicant's arguments regarding amended claim 51 now recites "a herpes virus genome" and no longer recites "the herpes virus genome" and overcomes the rejection for lack of antecedent basis of the recites phrase "the herpes virus genome" have been fully considered and found persuasive. Accordingly, the rejection of claim 51 in this aspect is ***withdrawn***.

7. Claims 16 and 17 remain rejected under 35 U.S.C. 112, second paragraph as there is insufficient antecedent basis for this limitation in the claim. Applicant's arguments have been fully considered and found not persuasive.

***Applicant's arguments*:** With regard to claims 16 and 17 being unclear for reciting "the absent region" which lacks antecedent basis, Applicant argues that the limitation "absent from the construct" of part (c) of claim 1 provides the antecedent basis of the limitation "the absent region" recited claim 16 and 17.

***In response:*** The limitation "the absent region" recited in claims 16 and 17 ***remains*** unclear because claim 1 is unclear when part (b) and part (c) are considered together. See the new 112 second rejection below in this office action.

8. Claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 37-41, and 45-53 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in limitation (b) "the viral genomic nucleic acid is from 1 to 50 kb in length", and in limitation (c) "more than 10% and up to 95% of the viral sequences which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct are absent from the construct". Considering the size of HSV-2, the elected invention for prosecution, being 152 kb, the limitation (c) with respect to the absence of 10% of a 152 kb HSV-2 genome, there will be 136.8 kb HSV genome remained. And the absence of 95% of a 152 kb HSV-2 genome, there will be 7.6 kb HSV genome remained. Accordingly, claim 1 recites two distinct different ranges of herpes virus genomic

nucleic acid: 1 to 50 kb (limitation (b)) and 7.6 to 136.8 kb (limitation (c)). Claims 3, 7-10, 12-14, 16-19, 21, 26-30, and 45-53 depend from claim 1.

Similarly, claim 37 recites in limitation (a) "said viral genomic nucleic acid being from 1 to 50 kb", and in limitation (b) "more than 10% and up to 95% of the viral sequences which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct are absent from the construct". Considering the size of HSV-2, the elected invention for prosecution, being 152 kb, the limitation (c) with respect to the absence of 10% of a 152 kb HSV-2 genome, there will be 136.8 kb HSV genome remained. And the absence of 95% of a 152 kb HSV-2 genome, there will be 7.6 kb HSV genome remained. Accordingly, claim 37 recites two distinct different ranges of herpes virus genomic nucleic acid: 1 to 50 kb (limitation (a)) and 7.6 to 136.8 kb (limitation (b)). Claims 38-41, depend from claim 37.

### *Claim Rejection - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 37-41, and 45-53 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Previous rejection is ***maintained*** for the reasons of record advanced on pages 8-10 of the office

action mailed on 04/19/2007. Previous rejection of claims 2 and 4 is moot because claims 2 and 4 have been canceled.

It is noted that the wild type genome of HSV, such as HSV-2 (recited in claim 19), is 152 kb and the specification of instant application does not disclose which portion of the 80% sequence homology to any given herpes viral genomic nucleic acid is to be selected for construction of the claimed isolated nucleic acid being 1 to 50 kb in length, which is recited in limitation (b) of claims 1 and 37, and being at the size of 7.6 kb to 136.8 kb, which is recited in limitation (c) of claim 1and limitation (b) of claim 37 (See discussions in section ***(i)*** of the preceding 112 second rejection).

***Applicant's arguments***

With regard to whether proper written description is disclosed in the specification regarding the limitation "a nucleic acid sequences that has at least 80% sequence homology to a herpes virus" in claim 1 and the limitation "at least 80% sequence homology" recited in claim 37, Applicant argues that it is apparent from the specification as a whole, especially in light of the prior art, that the inventors were in full possession of the invention at the priority date of the present application.

Applicant argues that, as discussed *supra*, the specification does not list the well-known HSV sequences as the skilled person would be aware of them. In support, Applicant states that Applicant has provided several references in the supplemental Information Disclosure Statement filed herewith, which disclose relevant sequences before the filing date of the present

application. Further, Applicant asserts that the HSV-2 sequence used in the present Examples was also known, as shown in the Genbank entry provided in the supplemental Information Disclosure Statement filed herewith. Therefore, inclusion of these sequences is unnecessary to show possession of the present invention.

Applicant also argues that evidence of information regarding the structure of other herpes virus genomes or its infectivity was well known in the art. Applicant argues that to satisfy the written description requirement, it is not necessary that the specification include such information that is already well-know in the art. Applicant indicates that, as shown in Dolan et al., submitted in the supplemental Information Disclosure Statement filed herewith, extensive comparisons between HSV types and strains had been published at the time of filing the present application; specifically, Dolan et al. compares HSV-1 and HSV-2 gene-by-gene and element-by-element in Tables 1 and 3, including the surface proteins important for infectivity. Applicant indicates that this reference also compares functional elements of the genome, such as the origin of replication on page 2011, first column. Further, this reference teaches the sequences of genes from various strains of HSV-2 in Table 2.

Applicant further argues that the specification describes how constructs of the invention can be generated in detail, and the description discusses in details over pages 34 to 41 how genomic fragments can be obtained from the genomes of viruses and how redundant sequences can be removed. Applicant asserts that these passages further illustrate that the inventors were in full possession of the invention and describe in detail how the invention can be put into practice in the specification.

With respect of the reference in the claims to sequences with at least 80% homology,

Applicant argues that, as discussed *supra*, the specification refers to appropriate methods for calculating sequence homology, and the inventors therefore illustrate how to identify fragments with appropriate sequence homology.

***Response to Applicant's Arguments***

The key issue of this rejection under 35 U.S.C. 112, first paragraph, written description, is hinged on the recitation of "a nucleic acid sequences that has at least 80% sequence homology to *a* herpes virus" in claim 1 and the recitation of "at least 80% sequence homology sequence homology" in claim 37, in the absence of written description regarding which portion of the 80% sequence homology to any given herpes virus genomic nucleic acid is to be selected for construction of the claimed isolated nucleic acid. Furthermore, the limitation "at least 80% sequence homology to *a* herpes virus genomic nucleic acid" recited in claim 1 encompasses any fragment of any herpes viral genomic nucleic acid sequences since the limitation is not limited solely to a full length virulent HSV genome. The specification fails to disclose the criteria used to determine which portion of the 80% sequence homology to any portion of any given herpes virus genomic nucleic acid is to be selected for construction of the claimed isolated nucleic acid.

As discussed in the 112 second rejection in this office action, part (b) of claim 1 recites "the viral genomic nucleic acid is from 1 to 50 kb in length" and part (c) of claim 1 recites the limitation "more than 10% and up to 95% of the viral sequences which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct are absent from the construct" are considered together given the size of HSV-2, the elected invention for prosecution, being 152 kb. Absence of 10% of a 152 kb HSV-2

genome will have 136.8 kb HSV genome remaining, and absence of 95% of a 152 kb HSV-2 genome will have 7.6 kb HSV genome remaining. Accordingly, claim 1 and its dependent claims are reciting two distinct different ranges of herpes virus genomic nucleic acid: 1 to 50 kb and 7.6 to 136.8 kb. Accordingly, since it is not even clear what size of a HSV genomic nucleic acid is encompassed the claims of instant application, claims 1, 3, 7-10, 12-14, 16-19, 21, 26-30, 37-41, and 45-53 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to the disclosure regarding preparation of viral genomic nucleic acid on pages 34-41 of the specification, the Examiner notes that the rejection is not based on the lack of written disclosure at technical levels how the viral genomic DNA can be isolated and purified, as disclosed on pages 34-41 of the specification. *Rather, it is the lack of written description regarding the criteria used to determine which fragment(s) of the 80% sequence homology to any given herpes viral genomic nucleic acid is to be selected for construction of the claimed isolated nucleic acid.* For instance, are the coding sequences of HSV genes, regulatory elements, sequences of unknown function, or some other un-specified genetically modified or naturally mutated sequences of a HSV genome, which has not been identified yet, to be included in the claimed isolated nucleic acid? The specification does not provide any specific guidance in this regard.

Regarding the breadth of the claims, because the metes and bounds of the length of recited viral genome cannot be determined as discussed in the rejection under 35 U.S.C. 112

second, it is worth emphasizing again that the limitation "at least 80% sequence homology to *a* herpes virus genomic nucleic acid" recited in claim 1 and the limitation " *a* sequence with at least 80% sequence homology into a vector backbone" recited in claim 37 encompass any fragment of any herpes viral genomic nucleic acid sequences since the limitation is not limited solely to a full length virulent HSV genome. To demonstrate this point, the breadth of the claims of instant application reads on the post-filing art published by **Terada et al., 2006** regarding construction of *mutant* oncolytic HSV vectors that express mouse IL4, CD40 ligand and 6CK via a novel BAC-based method designated as "HSVQuik system" (See abstract and Figure 1, Terada et al., Development of a rapid method to generate multiple oncolytic HSV vectors and their *in vivo* evaluation using syngeneic mouse tumor models, *Gene Ther.* 13(8):705-14, 2006). As an additional example, the breadth of the claims of instant application also reads on the post-filing art published by **Margolis et al., 2007** regarding *chimeric* HSV-2 mutant, that expresses the HSV-1 LAT (latency-associated transcript) and exhibited an HSV-1 phenotype, preferentially establishing latency in A5-positive neurons (See abstract, Margolis et al., Herpes simplex virus type 2 (HSV-2) establishes latent infection in a different population of ganglionic neurons than HSV-1: role of latency-associated transcripts. *J Virol.* 81(4):1872-8, 2007).

### *Claim Rejection - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Previous rejection of claims 1-4, 7-9, 12-14, 16, 17, 21, 26-30, 37-41, and 45-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Roizman et al. (Roizman, U.S. Patent Number: 5,288,641, issued Feb, 22, 1994) as evidenced by Leopardi et al. (U. S Patent number: 5,876,923, issued Mar. 2, 1999) is ***withdrawn*** because Applicant's arguments in combination with the claims amendments have been fully considered and found persuasive.

Applicant argues that Roizman et al. employs the whole HSV genome as a vector whereas the present invention employs vectors comprising fragments of an HSV genome. It is noted that the genome of wild type HSV-2 virus is 152 kb in size. In addition to the difference sizes between HSV taught by Roizman et al. and the claimed invention of instant application, the Examiner acknowledges that neither Roizman et al. nor Leopardi et al. teaches the amended limitation "at least two endogenous gene expression regulatory units which each comprise an endogenous promoter that is capable of expression in a mammalian cell, where the endogenous promoter of the units are all immediate early, all early or all late promoters", in the context of additional limitation recited in claims 1 and 37 stating that the viral genomic nucleic acid is from 1 to 50 kb in length.

## *Conclusion*

11. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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